

WO 98/40747

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FIGURE 1

LOCUS HSTGFB3M 2574 bp RNA PRI 12-SEP-1993
DEFINITION Human mRNA for transforming growth factor-beta 3 (TGF-beta 3).
ACCESSION X14149
NID g37095
KEYWORDS growth factor; transforming growth factor; transforming growth factor-beta 3.
SOURCE human.
ORGANISM Homo sapiens
Eukaryotae; mitochondrial eukaryotes; Metazoa; Chordata; Vertebrata; Eutheria; Primates; Catarrhini; Hominidae;
Homo.
REFERENCE 1 (bases 1 to 2574)
AUTHORS Chen, E.Y.
TITLE Direct Submission
JOURNAL Submitted (23-MAR-1989) Chen E.Y., Genentech Inc., 460 Pt. San Bruno Blvd., San Francisco, CA 94080, USA
REFERENCE 2 (bases 1 to 2574)
AUTHORS Derynck, R., Lindquist, P.B., Lee, A., Wen, D., Tamm, J., Graycar, J.L., Rhee, L., Mason, A.J., Miller, D.A., Coffey, R.J., Moses, H.L. and Chen, E.Y.
TITLE A new type of transforming growth factor-beta, TGF-beta 3
JOURNAL EMBO J. 7 (12), 3737-3743 (1988)
MEDLINE 89091120
COMMENT See <J03241> for alternative sequence of TGF-beta 3.
FEATURES
source Location/Qualifiers
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/db_xref="taxon:9606"
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/cell_line="A172 glioblastoma"
/chromosome="14q24"
CDS 254..1492
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/db_xref="SWISS-PROT:P10600"
/translation="MKMHLQRALVVLALLNLFATVSLSLSTCTTLDLFGHIKKRVEAIR
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SKRNEQRIELFQILRPDEHIAKQRYIGGKNLPTRGTAEWLSFDVTDTVREWLLRRESN
LGLEISIHCPCHTFQPNGDILENIHEVMEIKFKGVDNEDDHGRGDLGRLKKQKDHNP
HLILMMIPPHRLDNPQGQGRKKRALDTNYCFRNLENCVRPLYIDFRQDLGWKVVH
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GRTPKVEQLSNMVKCKCS"
BASE COUNT 629 a 680 c 666 g 599 t

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FIGURE 1 (cont'd)

ORIGIN

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121 caccttcttg ccaagcctca gtcttttggga tctggggagg ccgcctgggt ttcctccctc
181 cttctgcacg tctgctgggg tctcttctc tccaggcctt gccgtcccc tggcctctct
241 tcccagctca cacatgaaga tgcacttgca aagggtctct gtggtcctgg ccctgctgaa
301 ctttgccacg gtcagcctct ctctgtccac ttgcaccacc ttggacttcg gccacatcaa
361 gaagaagagg gtggaagcca ttaggggaca gatcttgagc aagctcaggc tcaccagccc
421 ccctgagcca acggtgatga cccacgtccc ctatcaggtc ctggcccttt acaacagcac
481 ccgggagctg ctggaggaga tgcattggga gagggaggaa ggctgcaccc aggaaaacac
541 cgagtcggaa tactatgcca aagaaatcca taaattcgac atgatccagg ggctggcgga
601 gcacaacgaa ctggctgtct gccctaaagg aattacctcc aaggttttcc gcttcaatgt
661 gtcctcagtg gagaaaaata gaaccaacct attccgagca gaattccggg tcttgccggg
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781 agatgagcac attgccaac agcgtctatat cgggtggcaag aatctgcccc cacggggcac
841 tgccgagtggt ctgtcctttg atgtcactga cactgtgctg gagggtgctg tgagaagaga
901 gtccaactta ggtctagaaa tcagcattca ctgtccatgt cacacctttc agcccaatgg
961 agatattcctg gaaaacattc acgaggtgat ggaaatcaaa ttcaaaggcg tggacaatga
1021 ggatgaccat ggccgtggag atctggggcg cctcaagaag cagaaggatc accacaaccc
1081 tcatctaata ctcatgatga ttccccaca ccggctcgac aacctggagg agaactgctg
1141 gaggaagaag cgggcttttg acaccaatta ctgcttccgc aacttggagg agaactgctg
1201 tgtgcgcccc ctctacattg acttccgaca ggaatctggg tggaagtggg tccatgaacc
1261 taagggtctac tatgccaact tctgtcagc cactctgaac cctgaagcat ctgcctcgcc
1321 aaccacagc acggtgctgg gactgtacaa cactctgaac cctgaagcat ctgcctcgcc
1381 ttgctgcgtg cccagggacc tggagccct gaccatctg tactatgttg ggaggacccc
1441 caaagtggag cagctctcca acatggtggt gaagtctgt aaatgtagt gagacccac
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1561 acacaagcaa caaacctcac tgagaggcct ggagcccaca accttcggct ccgggcaaat
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1681 ggtaaagaaa gtgtgggttt gggttagagga aggctgaact cttcagaaca cacagacttt
1741 ctgtgacgca gacagagggg atggggatag aggaaaggga tggtaagtgt agatgttgtg
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1981 acgaagacaa agtcccagaa ttgtatctca tactgtctgg gattaagggc aaatctatta
2041 cttttgcaaa ctgtcctcta catcaattaa catcgtgggt cactacaggg agaaaatcca
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2161 gaaagggttg aaatcaaccc tctcctgtct gccctctggg tccctcctct cacctctccc
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2281 tggattgttg ttccatgcag ccttggggca ttatgggtct tccccactt cccctccaag
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2401 agctgcacat gtgccacaca gtgacttggc cccagacgca tagactgagg tataaagaca
2461 agtatgaata ttactctcaa aatctttgta taaataaata tttttggggc atcctgggat
2521 atttcatctt ctggaatatt gtttctagaa cagtaaaagc cttattctaa ggtg

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FIGURE 2

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LOCUS HSU22431 3678 bp mRNA PRI 28-JUN-1995
DEFINITION Human hypoxia-inducible factor 1 alpha (HIF-1 alpha) mRNA, complete
cds.
ACCESSION U22431
NID g881345
KEYWORDS .
SOURCE human.
ORGANISM Homo sapiens
Eukaryotae; mitochondrial eukaryotes; Metazoa; Chordata;
Vertebrata; Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE 1 (bases 1 to 3678)
AUTHORS Wang, G.L., Jiang, B.H., Rue, E.A. and Semenza, G.L.
TITLE Hypoxia-inducible factor 1 is a basic-helix-loop-helix-PAS
heterodimer regulated by cellular O2 tension
JOURNAL Proc. Natl. Acad. Sci. U.S.A. 92 (12), 5510-5514 (1995)
MEDLINE 95296340
REFERENCE 2 (bases 1 to 3678)
AUTHORS Wang, G.L., Jiang, B.-H., Rue, E.A. and Semenza, G.L.
TITLE Direct Submission
JOURNAL Submitted (09-MAR-1995) Gregg L. Semenza, Center for Medical
Genetics, The Johns Hopkins University School of Medicine, 600 N.
Wolfe St., Baltimore, MD 21287-3914, USA
FEATURES Location/Qualifiers
source 1..3678
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/db_xref="taxon:9606"
/cell_line="Hep3B"
/cell_type="hepatoblastoma"
gene 29..2509
/gene="HIF-1 alpha"
CDS 29..2509
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/standard_name="hypoxia-inducible factor 1, alpha subunit"
/note="basic helix-loop-helix transcription factor"
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/product="hypoxia-inducible factor 1 alpha"
/db_xref="PID:g881345"
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CLVLICEPIPHPSNIEIPLDSKTFLSRHS LDMKFSYCDERITELMGYEPEELLGRSIY
EYYHALDS DHLT KTHHDMFTKGQVTTGQYRMLAKRGYVWVETQATVIYNTKNSQPQC
IVCVNYVVSGIIQHDLIFSLQQTECVLKPVESSDMKMTQLFTKVESED TSSLFDKLKK
EPDAL TLLAPAAGDTIISLDFGSNDTETDDQLEEVPLYNDVMLPSPNEKLQINLAM
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SSPEPNPSEYCFYVDS DMVNEFKLELVEKLFAEDTEAKNPFSTQDTDL DLEMLAPYI
PMDDDFQLRSFDQLSPLESSSASPESASPOSTVTVFQQTQIQEPTANATTTTATTTDEL
KTVTKDRMEDIKILIASPSPTHIHKETTSATSSPYRDTQSRTASPNRAGKGVIEQTEK
SHPRSPNVLSVALSQR TTVPEELNPKILALQNAQRKRKMEHDGSLFQAVGIGTLLQQ
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/note="42 A nucleotides"
BASE COUNT 1197 a 695 c 675 g 1111 t

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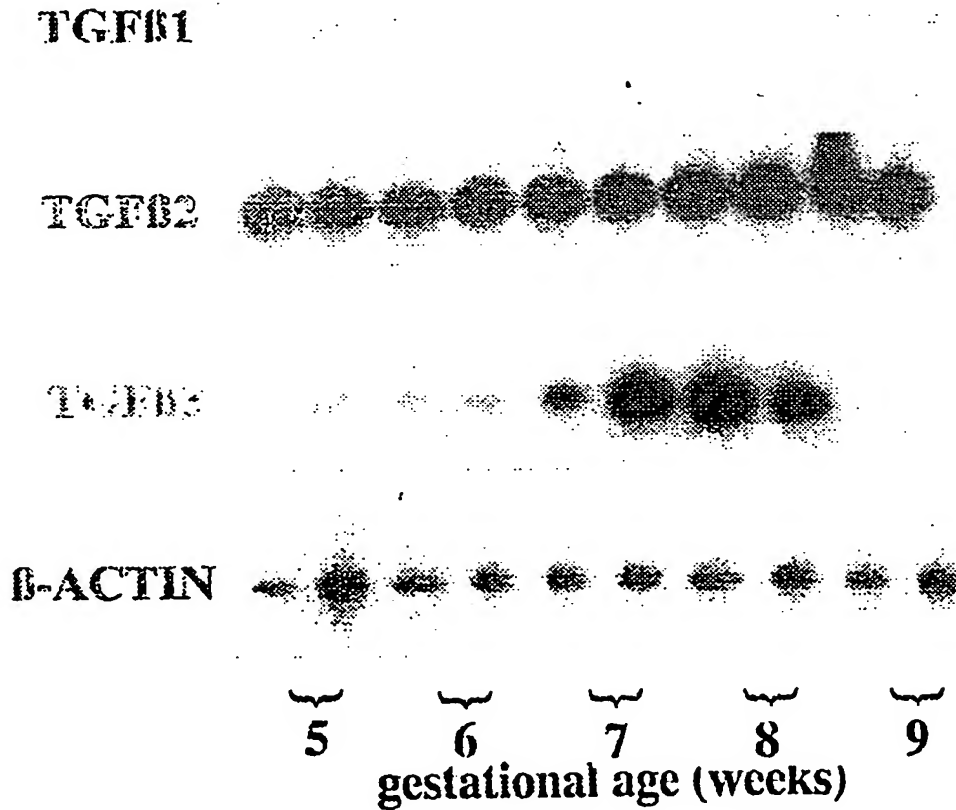
FIGURE 2 (cont'd)

ORIGIN

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241	acttctggat	gctggtgatt	tggatattga	agatgacatg	aaagcacaga	tgaattgctt
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361	catttctgat	aattgtgaaca	aatacatggg	attaactcag	tttgaactaa	ctggacacag
421	tgtgtttgat	tttactcatc	catgtgacca	tgaggaaatg	agagaaatgc	ttacacacag
481	aaatggcctt	gtgaaaaagg	gtaaaaaaca	aaacacacag	cgaagctttt	ttctcagaat
541	gaagtgtacc	ctaactagcc	gaggaagaac	tatgaacata	aagtctgcaa	catggaaggt
601	attgcactgc	acaggccaca	ttcacgtata	tgataccaac	agtaaccaac	ctcagtggtg
661	gtataagaaa	ccacctatga	cctgcttggg	gctgatttgt	gaacccattc	ctcaccatc
721	aaatattgaa	attccttttag	atagcaagac	tttctcagt	cgacacagcc	tggatatgaa
781	attttcttat	tgtgatgaaa	gaattaccga	attgatggga	tatgagccag	aagaactttt
841	aggccgctca	atttatgaat	attatcatgc	tttgactct	gatcatctga	ccaaaactca
901	tcattgatatg	tttactaaaq	gacaagtcac	cacaggacag	tacaggatgc	ttgcccataa
961	aggtggatat	gtctgggttg	aaactcaagc	aactgtcata	tataacacca	agaattctca
1021	accacagtgc	attgtatgtg	tgaattacgt	tgtgagtggg	attattcagc	acgacttgat
1081	tttctccctt	caacaaacag	aattgtgtcct	taaaaccggtt	gaatcttcag	atatgaaaat
1141	gactcagcta	ttcaccaaaq	ttgaatcaga	agatacaagt	agcctctttg	acaaacttaa
1201	gaaggaacct	gatgctttaa	ctttgctggc	cccagccgct	ggagacacaa	tcatatcttt
1261	agattttggc	agcaacgaca	cagaaactga	tgaccagcaa	cttgagggaag	taccattata
1321	taatgatgta	atgctccctt	cacccaacga	aaaattacag	aatataaatt	tggcaatgtc
1381	tccattaccc	accgctgaaa	cgccaaagcc	acttcgaagt	agtgtctgac	ctgcactcaa
1441	tcaagaagtt	gcattaaaaat	tagaaccaaa	tccagagtca	ctggaacttt	cttttaccat
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1561	tgagccataat	agtcaccagt	aatattgttt	ttatgtggat	agtgtatagg	tcaatgaatt
1621	caagttggaa	ttggtagaaa	aactttttgc	tgaagacaca	gaagcaagaa	acccattttc
1681	tactcaggac	acagattttag	acttgagatg	gttagctccc	tatatcccaa	tggatgatga
1741	cttccagtta	cgttcccttcg	atcagttgtc	accattagaa	agcagttccg	caagccctga
1801	aagcgcaagt	cctcaaagca	cagttacagt	attccagcag	actcaaatac	aagaacctac
1861	tgctaatgcc	ccactaccac	ctgccaccac	tgatgaatta	aaaacagtga	caaaagaccg
1921	tatggaagac	attaaaaatat	tgattgcac	tccatctcct	acccacatac	ataaagaaac
1981	tactagtgcc	acatcatcac	catatagaga	tactcaaagt	cggacagcct	caccaaacag
2041	agcaggaaaa	ggagtcatag	aaacagacaga	aaaatctcat	ccaagaagcc	ctaactgtgt
2101	atctgtcgct	ttgagctaaa	gaactacagt	tcttgaggaa	gaactaaatc	caaagatact
2161	agctttgcag	aatgctcaga	gaaagcgaaa	aatggaacat	gatggttcac	tttttcaagc
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2341	tatttttaata	ccctctgatt	tagcatgtag	actgctgggg	caatcaatgg	atgaaagtgg
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2461	cctactgcag	ggtgaagaat	tactcagagc	tttgatcaa	gttaactgag	ctttttctta
2521	atttcattcc	tttttttggg	cactggtggc	tcactaccta	aagcagctta	tttatatttt
2581	ctacatctaa	tttttagaagc	ctggctacaa	tactgcacaa	acttggttag	ttcaattttt
2641	gatccccctt	ctacttaatt	tacattaatg	ctctttttta	gtatgttctt	taatgctgga
2701	tcacagacag	ctcattttct	cagttttttg	gtatttaaac	cattgctattg	cagtagcatc
2761	atttttaaaaa	atgcaccttt	ttattttatt	atttttggct	agggagttta	tccttttttc
2821	gaattatttt	taagaagatg	ccaatataat	ttttgtaaga	aggcagtaac	ctttcatcat
2881	gatcataggc	agttgaaaaa	tttttacacc	ttttttttca	cattttacat	aaataataat
2941	gctttgcccag	cagtacgtgg	tagccacaat	tgcacaatat	attttcttaa	aaaataccag
3001	cagttactca	tggaatatat	tctgcgttta	taaaactagt	ttttaagaag	aaattttttt
3061	tggcctatga	aattgttaaa	cctggaacat	gacattgtta	atcatataat	aatgattctt
3121	aaatgctgta	tggtttatta	tttaaatggg	taaagccatt	tacataatat	agaaagatat
3181	gcataatatc	agaaggatg	tggcatttat	ttggataaaa	ttctcaattc	agagaaatca
3241	tctgatgttt	ctatagtcac	tttgccagct	caaaagaaaa	caactaccta	tgtagtgtg
3301	gaagtttatg	ctaattttgt	gtaactgata	ttaaacctaa	atgttctgac	taccctgttg
3361	gtataaagat	attttgagca	gactgtaaac	aagaaaaaaa	aaatcatgca	ttcttagcaa
3421	aattgcctag	tatgttaatt	tgtctaaaat	acaatgtttg	attttatgca	ctttgtcgct
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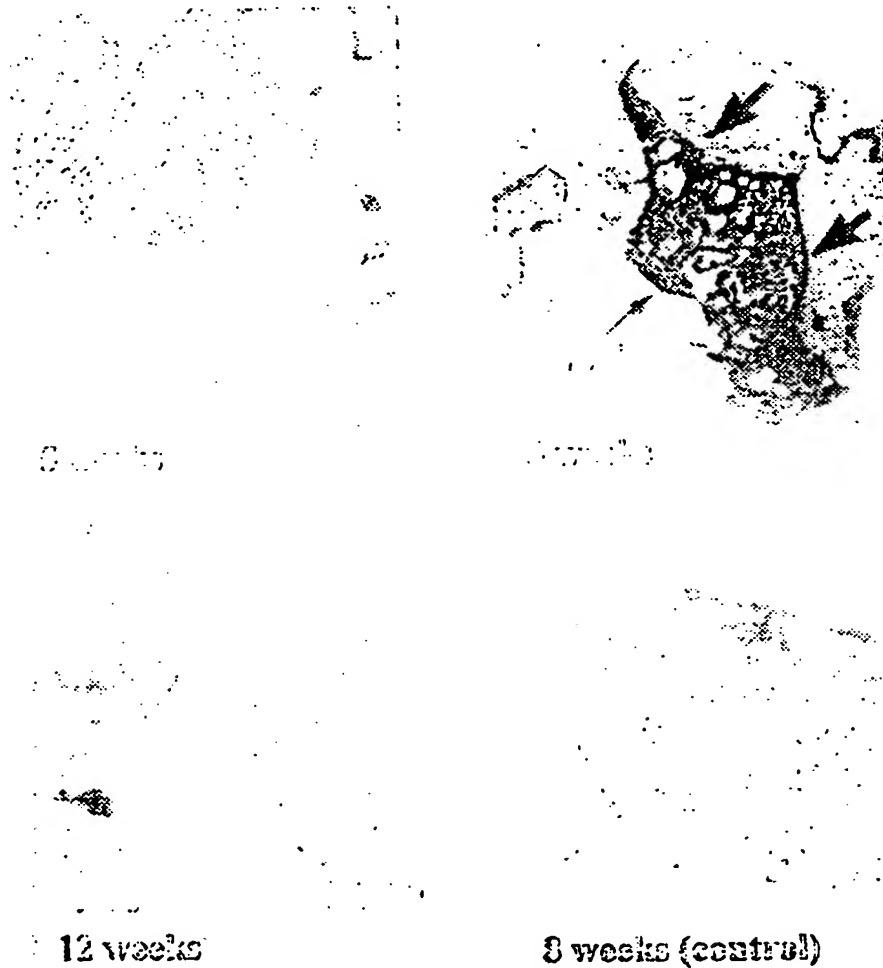
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FIGURE 3A



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FIGURE 3B

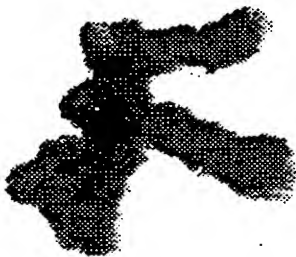


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FIGURE 4A

CONTROL



AS-B3



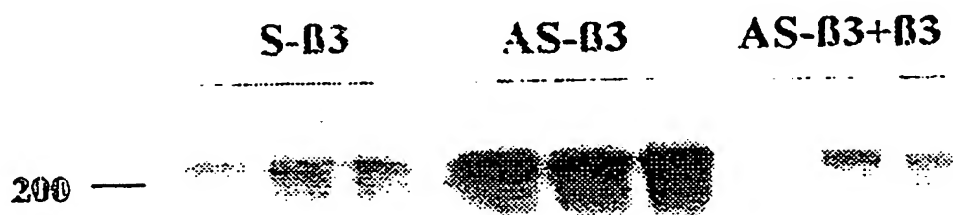
AS-B3 + B3



10028158 132001

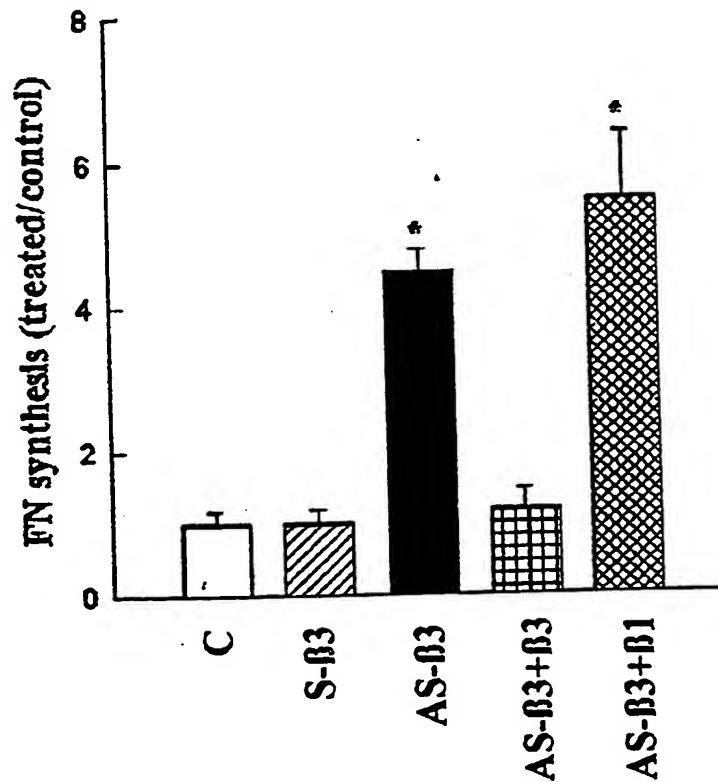
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FIGURE 4B



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FIGURE 4C

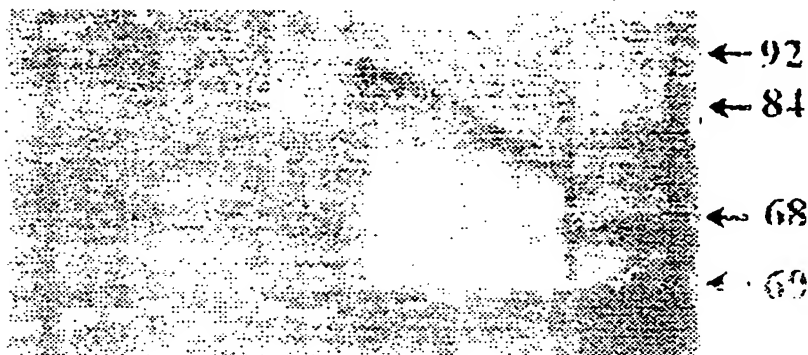


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FIGURE 4D

S-B3

AS-B3

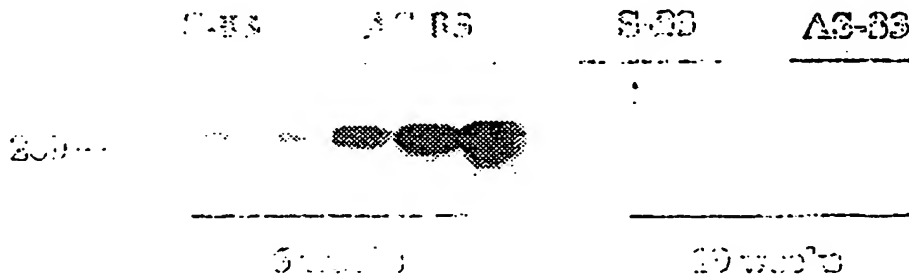


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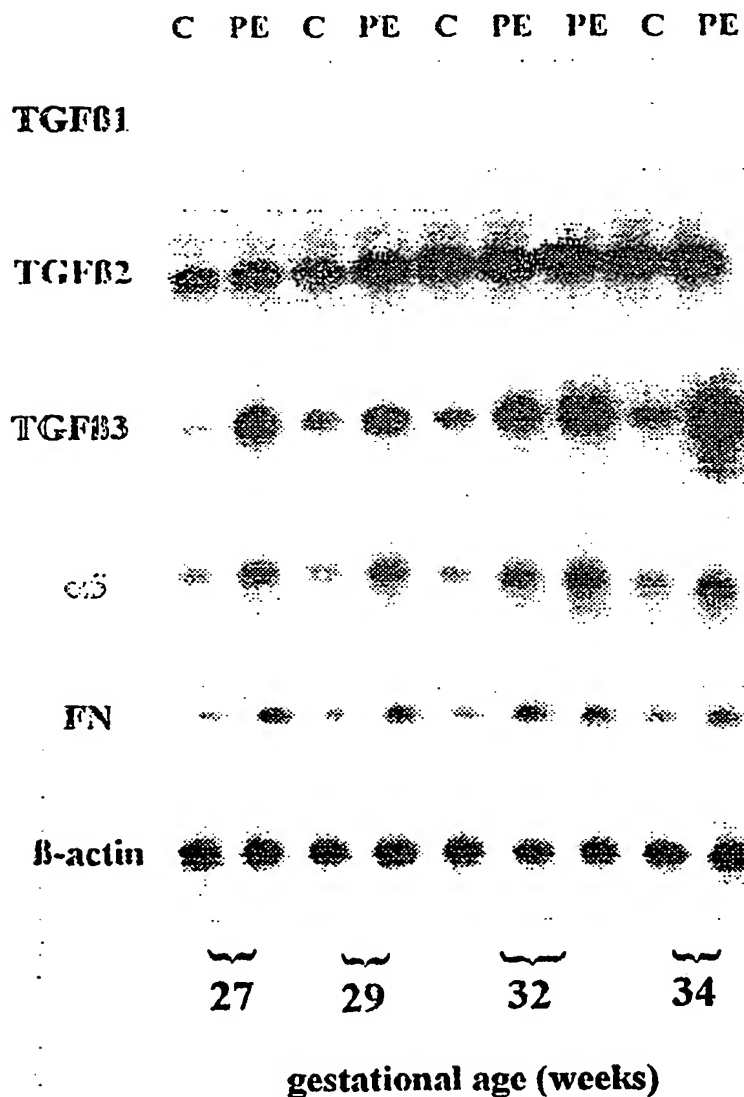
FIGURE 4E

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FIGURE 5A



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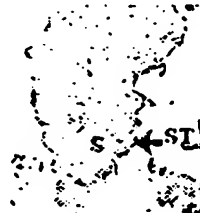
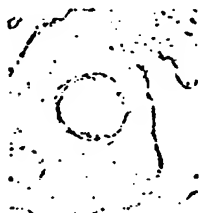
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FIGURE 5B

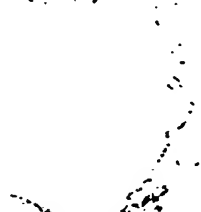
Normal Placenta

Preeclamptic Placenta

29 weeks



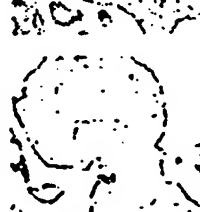
31 weeks



33 weeks



control



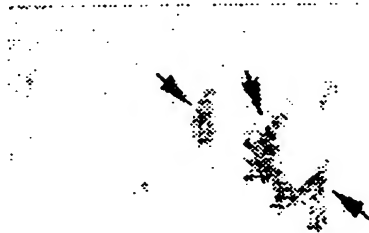
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FOOCT" 85T8200T

FIGURE 6A

Preeclamptic placenta



AS-B3



S-B3

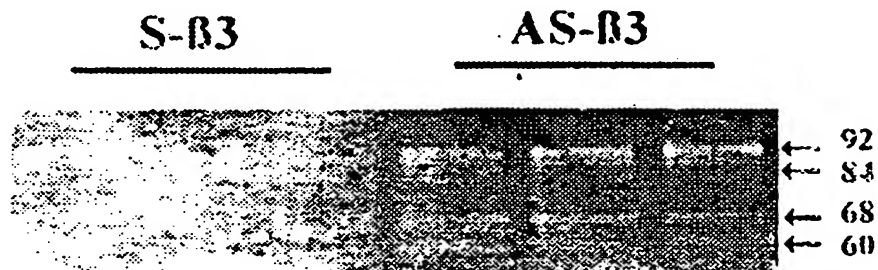
Normal placenta



S-B3

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FIGURE 6B



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FIGURE 6C

S-B3

AS-B3



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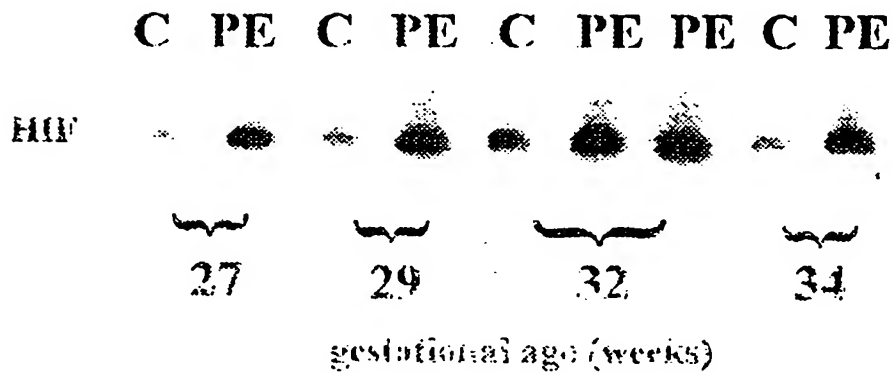
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FIGURE 7A

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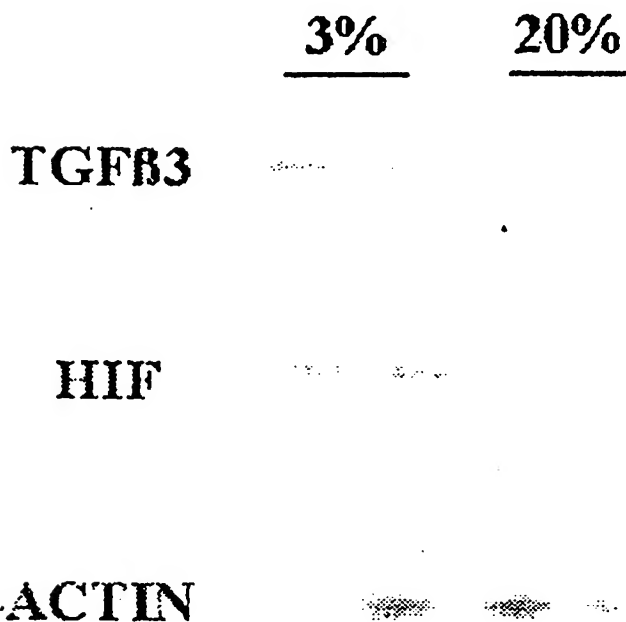
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FIGURE 7B



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FIGURE 8



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FIGURE 9

20% O₂



25X



50X

3% O₂



25X



50X

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FIGURE 10

